In the past year, researchers have reported killing cancer cells with magnetically driven, spinning iron–nickel discs; iron–cobalt particles; and radio waves aimed at gold, cadmium, indium, and gallium particles. It’s all happened in preclinical studies so far. But the studies have drawn attention, partly because of their science-fiction-sounding methods and partly because they highlight a burgeoning partnership between two unlikely bedfellows: materials science researchers and clinical oncologists.

“I’ve seen a dramatic increase over the last 3–4 years in the involvement of chemists, physicists, bioengineers, and materials scientists in clinical oncology,” said Steven Curley, M.D., a surgical oncologist at the M. D. Anderson Cancer Center in Houston, who is working on the radio waves.

Some of the partnerships are focused on nanoimaging devices (see accompanying news story); others, on nano- or microtherapeutics. The treatments they are exploring are diverse but share a core concept: the pairing of biologically active molecules such as drugs and antibodies with biologically inert particles such as metals and polymers.

**Magnetic Discs**
The research team in the study with magnetically driven iron–nickel discs included Maciej Lesniak, M.D., the neurosurgical oncology research director at the University of Chicago’s Pritzker School of Medicine, and materials science investigators Valentyyn Novosad, Ph.D., and Elena Rozhkova, Ph.D., from the Argonne National Laboratory near Chicago. Their discs, coated with glioma-specific interleukin 13 α2 receptor antibody, destroyed roughly 90% of human glioblastoma cells in vitro after just 10 minutes. The February 2010 cover of *Nature Materials* featured the study.

About 60 nm thick and 1 µm (i.e., micrometer, also called a micron) across, the discs spin under the influence of a weak magnetic field in the tumor cell microenvironment. Lesniak said that the spinning motion “compromises integrity for the cellular membrane and initiates programmed glioblastoma cell death.”

The iron–nickel discs appear to have fulfilled a 30-year-old promise that magnetic fields could selectively direct nanoscale particles to aggressive cancers. In the late 1970s, Northwestern University researchers Kenneth Widder, M.D., and Andrew Senyei, M.D., patented methods using magnetic particles to deliver chemotherapies. But tiny magnets often clump, an effect that gums up treatment channels and prevents manipulation by an outside magnetic field. Also, with most materials, the magnetic field strength falls off rapidly even small distances from target tissues, making impractically strong magnets necessary. The combination of iron and nickel solved both problems, keeping the discs from clumping and avoiding the need for superstrong magnetic fields.

The University of Chicago–Argonne team’s next goal is a phase I trial. In preparation, they are performing studies in multiple glioma cell lines, establishing animal models to verify efficacy, and doing U.S. Food and Drug Administration–directed toxicity studies, Lesniak said.

**Magnets and Metastases**
In another recent study, Georgia Institute of Technology researchers also used magnetic nanoparticles, this time to remove malignant cells from the ascites fluid of ovarian cancer patients. The particles are a cobalt–iron alloy coated with a tumor-specific peptide that attaches the particles to tumor cells. A magnet then removes the cells from the ascites (which collects as tumor cells are shed into the abdominal cavity).

The laboratory study offered the first in vitro demonstration that targeted nanoparticles can selectively remove metastasizing ovarian cancer cells from human peritoneal effusions, said Benedict Benigno, M.D., a gynecologic oncologist who heads Georgia Tech’s Ovarian Cancer Institute. The results appeared in the journal *Nanomedicine* in June.

The technique also has reduced metastasis in mice, according to coauthor John McDonald, Ph.D., chair of the biology department at Georgia Tech. He envisions a dialysis-type machine that filters abdominal fluids through a chamber where magnetic particles attach to the cancer cells and a magnetic trap filters them out. “The envisioned device could be easily incorporated into the well-established technique of circulating chemotherapeutic fluids through the abdomens of ovarian cancer patients after surgery,” Benigno added.

In the future, this approach could run into what nanotechnology and cancer researcher Steven Libutti, M.D., calls the “bedbugs and cockroaches” problem. “If you don’t get them all—the bugs or the cells—you’re going to get more,” said Libutti, who heads the Montefiore–Einstein
Center for Cancer Care at the Albert Einstein College of Medicine in Bronx, N.Y. “While you’re filtering peritoneal fluid, for instance, you can miss cells that have already escaped into other cavities.” To reduce this problem, the Georgia Tech team said their proposed method would be used in concert with systemic radiation and chemotherapies.

Radio Waves
A third technology, which uses radio waves, was the brainchild of a retired radio executive named John Kanzius and M. D. Anderson’s Curley. Their partnership developed when Kanzius, diagnosed with leukemia, proposed using radio waves to heat nanometer-sized metallic particles, which would then kill the cancer cells in a process called thermal cytotoxicity. Kanzius died in 2009, but by then he and Curley had developed the technique to the point that it could be tested in animal studies. The method conjugates cetuximab (Erbitux), a monoclonal antibody targeted at human epidermal growth factor receptor, to a variety of nanometer-sized metallic particles. The antibody delivers the particles to cancer cells that overexpress the receptor, and radio waves then heat the particles to kill the cells.

In a recent study in mice, the heated particles killed 70%–100% of pancreatic adenocarcinoma cells. The report appeared in the July 2010 issue of Cancer, and the mice were still alive with no signs of cancer 6 months after treatment. Notable side effects, Curley added, have been absent.

Curley said that although he won’t be satisfied until the technique works in humans, the results have “erased any doubts” about what he calls the Kanzius method. In preparation for human trials, Curley and colleagues are now studying new substrates and antibody markers for both pancreatic and hepatocellular cancers.

From Nano to Micro
Micrometer- rather than nanometer-sized particles are the focus of researchers at Ohio State University College of Pharmacy who are working with the larger particles to provide sustained paclitaxel as intraperitoneal
IP therapy during ovarian surgery. IP therapy has shown benefit in human trials, but local toxicity coupled with a higher risk of infection with IP catheters have kept it from becoming standard care. But according to an Ohio State study in mice, IP therapy with the tumor-penetrating micro-particles yielded 16-times-higher and more sustained paclitaxel concentrations, fewer toxic effects, less body weight loss, and longer survival than did IP with traditional chemotherapy drugs. The study, led by Jessie L. S. Au, Pharm.D., Ph.D., appeared in the *Journal of Pharmacology and Experimental Therapeutics* in December 2008.

Au’s team decided on micron- rather than nanometer-scale particles after comparing 13-nm-, 660-nm-, and micron-sized particles. They decided on an optimal size of about 4–5 microns, Au said, because the particle had to be “large enough to minimize rapid clearance through lymphatic drainage” yet “small enough to enable even distribution throughout the peritoneal cavity to reach tumors.” Nanometer-sized particles cleared too quickly, and “we found that larger particles on the order of 30 microns typically aggregate in the lower abdomen,” she added.

Such delivery considerations are major concerns, said Andrew Brenner, M.D., a medical oncologist at the University of Texas Cancer Therapy and Research Center in San Antonio, who is working on a method using nanoscale liposomal particles to deliver targeted radiotherapy. “It’s one thing to make these tiny particles but another thing to load and deliver them in such a way as to achieve a high enough and sustained concentration.”

The Ohio State researchers are now working with David Cole, M.D., at the Medical University of South Carolina department of surgery, to develop a phase I protocol to test their method in pancreatic cancer.

*Dr. Curley receives research funding from the Kanzius Cancer Research Foundation.*